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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,708	03/11/2005	Hideki Matsui	Q101073	9989

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EXAMINER	
SAJJADI, FEREYDOUN GHOTB	
ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,708	MATSUI ET AL.	
	Examiner	Art Unit	
	FEREYDOUN G. SAJJADI	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/4/2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15 and 51-53* is/are pending in the application.

4a) Of the above claim(s) *51-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Status

Applicants' response of March 2, 2009, to the non-final Office action dated June 12, 2008 has been entered. No claims have been amended, cancelled or newly added. Accordingly, claims 15 and 51-53 are pending in the Application. Claims 51-53 stand withdrawn from further consideration, without traverse, as drawn to non-elected inventions. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01. Claim 15 has been examined commensurate with the enabled scope previously indicated (i.e. a method comprising the step of hybridizing an antisense molecule or ribozyme to RNA of a gene encoding a protein comprising the amino acid sequence of SEQ ID NO: 1).

Claim 15 is under current examination.

Response & Maintained Claim Rejection - 35 USC § 112-Scope of Enablement

Claim 15 stands rejected under 35 U.S.C. §112, first paragraph, because the specification is not enabling for the full scope of the invention. The rejection set forth on pp. 7-12 of the Office action dated December 13, 2007, pp. 5-7 of the office action dated June 11, 2008, and pp. 3-4 of the previous Office action dated December 16, 2008 is maintained for claim 15, for reasons of record. Applicants have correctly indicated that claims 48-50 were previously cancelled.

The previous Office action indicated that the specification is considered only enabling for a method of screening for a compound or its salt that inhibits the expression of an RNA encoding a protein comprising the amino acid sequence set forth as SEQ ID NO: 1, said method comprising introducing into a nerve cell an antisense molecule or ribozyme to RNA of a gene encoding a protein comprising the amino acid sequence set forth as SEQ ID NO: 1, thereby

inhibiting the function of said RNA and inhibiting the neurofibrillary degenerating promoting activity of said protein.

Applicants disagree with the rejection, arguing that Applicants teach the importance of NIPK, a kinase, and drug candidate compounds thereof in neural biophysiological processes; and Applicants' specification and the state of the art is replete with examples of means by which to obtain drug candidate compounds to NIPK; therefore one having ordinary skill in the art conducting routine experimentation could practice the method. Applicants' arguments have been fully considered, but are not found persuasive.

In response, it should be noted that the issue is not the ability to screen for a compound that inhibits a kinase, *per se*, but rather, the ability to culture any type of cell comprising NIPK (neural cell death inducible putative kinase), including non-neural cells and further assaying the degree of changes in nerve fibers to determine neurofibrillary degeneration activity. Thus, the issues are specifically related to the nature of the putative kinase in regulating nerve fiber generation, and not to the general kinase assays cited by Applicants as exemplifying routine experimentation. None of the examples cited by Applicants as exemplifying the state of the art are specifically related to the expression of NIPK in non-neural cells and the assay for nerve fiber generation.

Applicants argue that at page 4 of the Office action, the Examiner alleges that numerous examples are required in order to satisfy the enablement requirement.

In response, it should be noted that the examiner made no such requirement. The Examiner indicated: "Instant claim 15 encompasses the inhibition of gene expression by any type of drug candidate compound. Further, the method is directed to the culture of any cell type comprising SEQ ID NO: 1, that include non-neuronal cells. Thus, it is not clear how the amendment of the claim has overcome the grounds of the rejection, as the claim clearly encompasses a broader scope than that originally presented, wherein the method was limited to using a polynucleotide. Moreover, it should be noted that the claimed method reads on any cell type, for example a fibroblast comprising the sequence of SEQ ID NO: 1, that would not exhibit any nerve fibers. As previously noted, the inhibition of gene expression includes inhibition of

promoter function either directly, or indirectly by inhibition of transcription factors. The instant specification, while teaching the amino acid of human neuronal cell death inducible putative kinase (NIPK, SEQ ID NO: 1), and the base sequence of DNA encoding the same (SEQ ID NO: 2, p. 69), fails to provide any information regarding the promoter sequences of genomic structure of the human NIPK gene. The specification if further silent on the transcription machinery controlling the expression of human NIPK, and additionally silent on how the transcription of the gene may be inhibited by a candidate compound. Thus, a person of skill in the art would need to engage in further experimentation to discover and characterize the transcription machinery of the human NIPK gene and the sequences controlling promoter activity to design a compound screening method to discover inhibitors of the human NIPK transcription machinery. Such experimentation thus constituting an undue burden on the skilled artisan."

Applicants should further note that the amount of direction or guidance presented in the specification and the presence or absence of working examples are both factors to be considered in a *Wands* analysis for enablement.

Applicants argue that even if a single claimed embodiment is inoperable (i.e. a fibroblast), the inoperability of a single embodiment does not warrant a finding that the specification fails to enable the claims under 35 U.S.C. § 112, first paragraph, citing *Atlas Power Co. v. E.I. du Pont de Nemours & Co.*

Such is not found persuasive, because a single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements. *In re Vickers*, 141 F.2d 522, 526-27, 61 USPQ 122, 127 (CCPA 1944); *In re Cook*, 439 F.2d 730, 734, 169 USPQ 298, 301 (CCPA 1971). However, in applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. *In re Soll*, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513

(Fed. Cir. 1993); *In re Vaeck*, 947 F.2d488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work.

Thus, the rejection is maintained for reasons of record and the preceding discussion.

Response & Maintained Claim Rejection - 35 USC § 103

Claim 15 stands rejected under 35 U.S.C. §103(a) as being unpatentable over Meyers et al. (U.S. Patent Application Publication No.: 2002/0034780; filed: Mar. 6, 2001), in view of Holocomb et al. (Dev. Biol. 172:307-323; 1995). The rejection set forth on pp. 5-7 of the previous Office action dated December 16, 2008 is maintained for reasons of record.

The Rejection:

The rejection has been applied to the extent that the instant claim encompasses an enabled method of screening for a compound or its salt that inhibits the expression of an RNA encoding a protein comprising the amino acid sequence set forth as SEQ ID NO: 1, said method comprising introducing into a nerve cell an antisense molecule or ribozyme to RNA of a gene encoding a protein comprising the amino acid sequence set forth as SEQ ID NO: 1, thereby inhibiting the function of said RNA and inhibiting the neurofibrillary degenerating promoting activity of said protein.

Meyers et al. describe human kinase nucleic acid sequences and proteins, and methods of using the same (Title and Abstract). Specifically disclosing in Figures 3A and 3B, the amino acid sequences of a human kinase protein (SEQ ID NO: 8), and its corresponding nucleotide sequence (SEQ ID NO: 9), the protein having 100% identity to the instantly claimed SEQ ID NO: 1. The kinase encoded by SEQ ID NO: 8 (also referred to as 13302 protein kinase [¶ 0062]), was found to be similar to rat NIPK neuronal cell-death-inducible putative kinase [¶ 0098]. Meyers et al additionally provide screening methods for identifying a compound that modulates the activity of the kinase protein as well as identifying a compound that modulates the expression of the kinase gene [¶¶ 0022-0024], wherein the compound or agent is a nucleic acid molecule having a nucleotide sequence that is antisense to the coding strand of the kinase mRNA or the kinase gene [¶ 0019]. The antisense nucleic acid molecules, are described as "molecules that are

complementary to a sense nucleic acid encoding a protein, e.g., complementary to the coding strand of a double-stranded cDNA molecule, or complementary to an mRNA sequence. Accordingly, an antisense nucleic acid can hydrogen bond to a sense nucleic acid. The antisense nucleic acid can be complementary to an entire kinase coding strand, or to only a portion thereof, e.g., all or part of the protein coding region (or open reading frame)" [¶ 0180]. Further teaching: "The invention also encompasses ribozymes, which are catalytic RNA molecules with ribonuclease activity that are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Ribozymes (e.g., hammerhead ribozymes (described in Haselhoff and Gerlach (1988) Nature 334:585-591)) can be used to catalytically cleave kinase mRNA transcripts to thereby inhibit translation of kinase mRNA. A ribozyme having specificity for a kinase-encoding nucleic acid can be designed based upon the nucleotide sequence of a kinase cDNA disclosed herein e.g., SEQ ID NOS: 1, 3, 4, 6, 7, 9" [¶ 0185]. Myers et al. additionally describe disorders involving the pancreas as including those of the exocrine pancreas such as diabetes mellitus ¶ [0138], and disorders involving the brain that include, but are not limited to, disorders involving neurons, and disorders involving glia, such as astrocytes, oligodendrocytes, ependymal cells, and microglia ¶ [0122].

While Myers et al. do not describe assaying the degree of neurofibrillary degeneration in their antisense compound screening method, such was known in the prior art.

Holocomb et al. describe the examination of apoptosis in the olfactory epithelium of the mouse and the regulation of neural number (Title and Abstract). Holocomb et al. further describe *in vitro* culture of neuronal cells and the assessment of their viability using calcein AM staining (as described on p., 32 of the instant specification), and the comparison of neural cell axons in the presence and absence of an apoptotic death inhibitor (Fig. 7, p.317); the axons representing nerve fibers.

The teachings of Meyers et al. and Holcomb et al. all encompass apoptosis inhibitors and their involvement in neurons. Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art, to combine their respective teachings and to apply the neural apoptosis monitoring and determination method of Holocomb et al., to the compound screening method of Meyers et al., as instantly claimed, with a reasonable expectation of success, at the time of the

instant invention. A person of ordinary skill in the art would have been motivated to utilize apoptosis determination method of Holocomb et al. in the method of Meyers et al., because such would allow for the assessment of the effectiveness of the apoptosis inhibitor in neural cell survival.

Applicants should note that the limitation wherein the compound or its salt is a candidate for a prophylactic or therapeutic agent for neurodegenerative disease or diabetes is not afforded patentable weight, because a drug compound may be a candidate for any disease and will remain nothing more than a candidate until proven otherwise. Thus, the limitation of a compound being a candidate for a disease amounts to nothing more than an intended use for the compound. As stated in MPEP 2106, II. Language that suggests or makes optional but does not require steps to be performed or does not limit a claim to a particular structure does not limit the scope of a claim or claim limitation. An example of such language includes statements of intended use.

Response to Arguments:

Applicants disagree, arguing that the Examiner failed to provide a sufficient reason or explicit analysis of why the disclosures of the references should be combined; that there is no suggestion to combine the teachings and suggestions of Meyers et al. and Holocomb et al., and that the Examiner, used Applicants' invention as a template through a hindsight reconstruction of claim 15. Applicants' arguments have been fully considered, but are not found persuasive.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

As indicated above, Meyers et al. describe human kinase nucleic acid sequences encoding the protein having 100% identity to the instantly claimed SEQ ID NO: 1. The kinase encoded by

SEQ ID NO: 8 (also referred to as 13302 protein kinase [¶ 0062]), was found to be similar to rat NIPK neuronal cell-death-inducible putative kinase [¶ 0098]. Meyers et al additionally provide screening methods for identifying a compound that modulates the activity of the kinase protein as well as identifying a compound that modulates the expression of the kinase gene [¶¶ 0022-0024], wherein the compound or agent is a nucleic acid molecule having a nucleotide sequence that is antisense to the coding strand of the kinase mRNA or the kinase gene [¶ 0019]. Myers et al. additionally describe disorders involving the brain that include, but are not limited to, disorders involving neurons, and disorders involving glia, such as astrocytes, oligodendrocytes, ependymal cells, and microglia ¶ [0122]. Thus, the only deficiency in Myers et al. is assaying for the degree of neurofibrillary degeneration following administration of the antisense compound that modulates the activity of the kinase. Such deficiency is cured by the teachings of Holocomb et al. describing *in vitro* culture of neuronal cells and the assessment of their viability using calcein AM staining (as described on p. 32 of the instant specification), and the comparison of neural cell axons in the presence and absence of an apoptotic death inhibitor (Fig. 7, p.317); the axons representing nerve fibers.

Therefore the teaching for assaying of neural cell axons was present in the prior art of Holocomb et al. and was not gleaned from Applicants' disclosure, as alleged by Applicants. The assay method of Holocomb et al. would be applicable by a person of ordinary skill in the art to any neural cell treated with an inhibitory compound. None the less, the previous Office action noted that the teachings of Meyers et al. and Holcomb et al. encompass apoptosis inhibitors and their involvement in neurons. Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art, to combine their respective teachings and to apply the neural apoptosis monitoring and determination method of Holocomb et al., to the compound screening method of Meyers et al., as instantly claimed, with a reasonable expectation of success, at the time of the instant invention. A person of ordinary skill in the art would have been motivated to utilize apoptosis determination method of Holocomb et al. in the method of Meyers et al., because such would allow for the assessment of the effectiveness of the apoptosis inhibitor in neural cell survival.

Thus, the rejection is maintained for reasons of record and the foregoing commentary.

Conclusion

Claim 15 is not allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR§1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FEREYDOUN G. SAJJADI whose telephone number is (571)272-3311. The examiner can normally be reached on 6:30 AM-3:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Fereydoun G Sajjadi/
Primary Examiner, Art Unit 1633